

EXHIBIT A

SUBSTITUTE SPECIFICATION

Solubilizates of essential oils and other substances

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In the processing for the integration of active
agents and additives in the end products in the
foodstuff, cosmetic and pharmaceutical sector as well
as in the nutrient solutions for cells or bacterial
10 cultures, stable, homogeneous, fine distribution of
the active agents or additives in the respective end
product stands in foreground due to reasons of
production technology, safety and practicability in
the applications, compliance with the legal
15 regulations as well as visual appearance.

Besides the stability of the homogeneity, which
must often be guaranteed for several years, optimally
fine distribution of the active substances or
20 additives in smallest volume units of the respective
end products plays a decisive role. The integration of
the water soluble active agents or additives in the
water-containing end products is in general possible
with finest distribution of particles.

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In contrast to that the integration of the active
agents or additives, which are fat-soluble and are not
soluble, or soluble with difficulty, in water, into
the end products represents, a problem from the

physical viewpoint, because such active agents or additives can be integrated in the end products for the purpose of achieving homogeneous distribution only after the corresponding time-consuming and elaborate
5 matrix design (oil/oil mixture or oil/water emulsion).

In order, for instance, to integrate, a fat-soluble substance such as retinol or beta carotene (daily requirement about 2 mg/day) into a quantity of
10 the end product, which is consumed or applied in a day, the volume of these small quantities of retinol or P-carotene must be increased through undesirable addition of a disproportionately large quantity of oil, so that an optimally homogeneous distribution can
15 be ensured in the end product.

However, this expansion of the volume, undesirable but necessary due to physical reasons, of the aforementioned substances for the purpose of achieving
20 homogeneous distribution in the end products is technologically essential both in the foodstuff as well as in the cosmetic and pharmaceutical products.

The oil-water emulsion of these substances for the
25 purpose of integration into the end products is not less elaborate, whereby, due to the particle size of at least 1 μ in the emulsion, no optimally fine distribution in the end product is possible. Apart from the fact that the substances that are not
30 soluble, or soluble with difficulty, in water, lead to problems in the processing for reasons mentioned above, and can result in poor homogeneity, these substances, incorporated in oil/oil mixtures or

oil/water emulsions, can be resorbed only to a limited extent.

5 The underlying problem of the invention is to
integrate substances that are not soluble in water, or
soluble in water with difficulty, so that, following
their addition into water or oil, they give a clear
solution and can be integrated in foodstuff, cosmetic,
pharmaceutical or nutrient solutions with finest
10 homogeneous distribution.

 To that end, the intention of the invention is to
provide a concentrate, which consists of an active
agent from the group, comprising an algae oil, an
essential oil, a terpene, phosphatidylserine, a co-3-
15 fatty acid, lanolin, conjugated linoleic acid
triglyceride, a citral and tea tree oil and a surplus
of polysorbate. Possibly addition of glycerol to the
mixture may also come in question. Especially
preferred is the use of polysorbate 80, however, in
20 the essential oils, of polysorbate 20. The
concentrates, according to the invention, of the
substances, for which the preferred compositions are
given in detail in the dependent claims, have proved
to be very effective and reliable.

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 Concentrates according to the invention that are
without moisture but soluble in water, can be
obtained, for example, by mixing the relevant active
agent with a surplus of polysorbate 80 or polysorbate
30 20 and stirring the mixture until it is clear. To
accelerate the mixing process, it is recommended to

heat the mixture to a temperature of approximately 80°C to approximately 100°C.

5 The active agent is micelled in this manner,
whereby the individual micelles have a size of not
greater than about 40 nm. With this micelling, the
resorption and the penetration of the substance uptake
in the respective digestive tract or skin is
substantially enhanced. The concentrates according to
10 the invention are easily soluble in water. To
accelerate the dissolution into water, it is
recommended to stir water, mildly heated to
approximately 40°C, into the concentrate.

15 The concentrates according to the invention find
application as additives to foodstuffs, in particular
to non-alcoholic drinks, in cosmetic products as
additives to salves and similar personal hygiene
products, as additives to pharmaceutical preparations
or nutrient solutions.

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The invention is explained on the basis of the
following exemplary instances.

Example 1 (Algae oil solubilizate):

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Material

a) An algae oil with proportion of about 45% of DHA
(ω3-fatty acid C 22:6) according to the following
DHActive Specifications:

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General Characteristics

	Description:	Vegetable oil from microalgae, containing approx. 45 % docosahexaenoic acid (DHA)
	Composition:	Triacylglycerols (> 95%)
5	Appearance:	Light waxy to fluid
	Color:	Light yellow
	Odor:	Characteristic
	Taste:	Characteristic

10 Fatty Acid Composition

22:6 DHA 43-50 %

Chemical Characteristics

	Free fatty acids	< 0.1 %
15	Peroxide value	< 5.0 meq./kg
	Unsaponifiabiles	< 2.0 %

Miscellaneous

	Proteins	< 0.1 %
20	Hexane	< 1.0 ppm

Elemental composition

	Arsenic	< 0.5 ppm
	Lead	< 0.1 ppm
25	Mercury	< 0.5 ppm

Antioxidant

Mixed natural tocopherols (1000 ppm added)
b) Polysorbate 80

160 g algae oil is mixed with 804 g polysorbate 80 until the mixture is clear or has homogeneous distribution and stirred until it is clear. To

accelerate the mixing process, the mixture is heated up to approximately 80°C. The solubilizate prepared in this manner contains 7% w/w of DHA (=docosahexaenoic acid). After completion of the mixing process, the mixture is cooled again and filled flushing it with nitrogen with exclusion of air oxygen and packed. If a polysorbate other than polysorbate 80 is used, the mixing ratio necessary for achieving the desired clearness of the mixture changes.

The solubilizate prepared in this manner can be dissolved in water giving a stable and clear solution. To accelerate the process of the dissolution into water, the concentrate and the water can preferably be heated to approximately 40°C to approximately 45°C. 2 g of this solubilizate covers the daily requirement of DHA (ω -3-fatty acid).

In place of algae oil, an ω -3-fatty acid containing animal fat, for example, one with 50% w/w DMA (docosahexanoic acid = C22:6), 10 w/w % EPA (eicosapentaenoic acid = C20:5) and 20 w/w% DPA (docosapentaenoic = C22:5n3). In the latter case, 210 g of this animal fat and 790 g of polysorbate 80 are processed into a concentrate as described above for algae oil. A water-soluble concentrate prepared in this manner contains 12% w/w of ω -3-fatty acids. To dissolve this concentrate in water, the concentrate must be first diluted with water at approximately 45°C in ratio by weight of about 1:2. After the solution becomes clear, it can be arbitrarily diluted without impairment

of the clearness. 1.2 g of this concentrate covers the daily requirement of ω -3-fatty acids.

If a polysorbate other than polysorbate 80 is used,
5 the proportions by weight of the concentrate change for achieving the desired clearness.

Example 2 (Essential oil solubilizte):

Material:

10 a) A natural orange oil named NATURE and obtained from the company Tutto Bianco, and having the following characteristics, as provided by the manufacturer "NATURE Der grüne Zweig von TUTTO BIANCO".

15 1. Product:

1.1 Article No.: A087

1.2 Charge No.: V003022

1.3 Trade name: Orange oil sweet

1.4 Origin: Brazil

20 1.5 Synonym: Aurantii dulcis aetheroleum

1.6 Pharmacopoeia: BP

2. Properties:

2.1 Color: Clear, brownish yellow to reddish
25 brown

2.2 Odor: Like sweet orange

2.3 Taste: Mild and aromatic

2.4 Consistency: Fluid

30 3. Identity

3.1 Gas chromatography: see below

4. Purity

	4.1	Soluble in ethanol 90%	1:7 v/v not always clearly soluble
	4.2	Miscible with	
	4.3	Relative density 20°C	0.8460
5	4.4	Refractive index 20°C	1.4730
	4.5	Optical rotation 20°C	+95°
	4.6	Acid number	1
	4.7	Alkaline and acidic reacting substance	
	4.8	Ester number	
10	4.9	Saponification number	
	4.10	External esters	corresponding
	4.11	Fatty oils	corresponding
	4.12	Resinified essential oils	corresponding
	4.13	Water soluble proportion	corresponding
15	4.14	Nonvolatile proportion	3% (= evaporation residue)
	4.15	Solidification point	
	4.16	Organic halogen compounds	not detectable
	4.17	Heavy metals	not detectable
20	4.18	Aldehyde content	2%

Analysis results of Gas Chromatography:

	0.5693%	n-Decylaldehyde
25	0.3359%	Anthranilic acid
	2.0178%	Myrcene
	95.757%	D+ Limonene
	0.4646%	Linalool

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b) Polysorbate 20

An essential oil, such as, for instance, 100 g orange oil, is stirred with 900 g polysorbate 20, until the mixture becomes clear or has homogeneous distribution. To accelerate the mixing process, the mixture can be heated, for instance, up to 80°C. A 10% orange oil concentrate prepared in this manner can be dissolved in water in any arbitrary mixing ratio. In order to accelerate the mixing process with water, the concentrate can be introduced into water heated to about 40°C and dissolved.

If one can do without clearness and the solubilizate can be used for other applications such as, for instance, for clear non-alcoholic drinks, the ratio by weight of the essential oil to polysorbate 20 can be adjusted, for instance, to 3:7. If a polysorbate other than polysorbate 20 is used, the proportions by weight in the concentrate necessary for achieving the required clearness change.

Orange oil concentrate with higher concentration is obtained, if about 850 g of polysorbate 20 are heated to about 50°C to about 60°C and in this warm polysorbate 20, about 150 g of the aforementioned orange oil is integrated under stirring. It is recommendable to heat the mixture again to about 85°C and stir it until it is transparent. The 15% orange oil concentrate thus obtained has light orange-yellow color, it is transparent and viscous and has a distinct orange odor. To obtain an aqueous solution of this concentrate, the best procedure is to stir with water at about 37°C ~~warm~~. A concentrate heated to this temperature can easily be processed as desired.

In analogous manner, orange oil concentrates with 10% w/w and 15% w/w can be prepared, if the respective introduced quantity of polysorbate 20 is changed accordingly and possibly stirred under mild heat. The concentrates can be used as a flavor in the production of ice cream, chewing gum and in food supplements.

The orange oil serves here solely as an example of an essential oil. In place of orange oil, other essential oils, such as, for example, tea tree oil can be used and solubilized:

Material:

a) Tea tree oil (MELALEUCA ETHEROLEUM) according to the following Analysis of "NATURE Der grüne Zweig von TUTTO BIANCO"..

MEAN RESULTS OF THE ANALYSIS

1. Product
 - 1.1 Trade name: Tee tree oil
 - 1.2 Article number: A113
 - 1.3 Synonym: MELALEUCA
Synonym: ETHEROLEUM
 - 1.4 Pharmacopoeia: Ph-Eur-4.01
EIEECS No. 85085-46-9; CTFA: Tea Tree Oil
Melaleuca alternifolia
2. Properties
 - 2.1 Color: colorless to weakly yellowish
 - 2.2 Odor: terpene like characteristic
 - 2.3 Taste
 - 2.4 Consistency: clear, liquid

3. Purity

3.1 Soluble in ethanol v/v%

3.2 Miscible with: Ethanol 96%, ether, fatty oils

5 3.3 Relative density 20 degrees C 0.8950

3.4 Refractive index 20 degrees C 1.4790

3.5 Optical rotation 20 degrees C +10°

3.23 Shelf life after delivery date: 24 months

3.24 Store with protection against light/air/heat

10 3.25 Origin: Australia

4. Identity

4.1 Chromatographic profile corresponding

4.2 Analysis results corresponding

15 4.3 CHARGE No. 040051

Allergenes contained in the natural
ingredients:

20 3% d-Limonene

AS-No.: 5989-27-5 EINECS-No: 227-
813-5

25

b) Polysorbate 20

About 700 g of polysorbate 20 are heated to
between approximately 50°C to approximately 60°C.

30 About 300 g of tea tree oil is stirred into the warm
polysorbate. The mixture is heated to approximately
85°C and stirred until the concentrate becomes clear:

The concentrate is transparent at room temperature, viscous and smells like tea tree oil. This 30% tea tree oil concentrate is water soluble.

5 To improve the solubility, it is recommendable to stir the concentrate in about 40°C warm water, following which a clear aqueous solution of the concentrate is obtained.

10 If a different polysorbate is used, the quantity of polysorbate and tea tree oil must be changed to obtain a clear concentrate.

15 Example 3 (γ -terpine solubilizate):

Material:

a) γ -terpines, having the following properties:

20 Date: 11.02.03
 Article number: 8039
 Product: γ -terpines ROTICHROM® GC
 Charge: 43256376
 Density: 0.849
 Formula: $C_{10}H_{16}$
25 Melting point: Flashpoint: 51°C
 CAS Number: 99-85-4
 Molecular weight: 136.24
 Storing temperature: +4°C
 Boiling point: 182°C
30 Project: defproj
 Instrument: channel4

Analysis: roth4

Sample: Gamma-terpines

Injection: 1

5	Peak Information		
	Uncorrected RT	Area	Area & Peak Name
	12.39 14.30	0.28	
	13.94 5031.02	91.28	
	14.25 39.39	0.71	
10	14.60 255.73	4.64	
	17.02 15.04	0.27	
	18.59 8.25	0.15	
	18.73 5.28	0.10	
	19.05 20.79	0.38	
15	20.10 8.72	0.15	
	20.20 5.17	0.09	
	20.38 15.53	0.28	
	20.77 7.72	0.14	
	21.70 2.92	0.05	
20	23.84 9.36	0.17	
	24.52 4.11	0.07	
	24.89 17.30	0.31	
	25.15 4.80	0.09	

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b) Polysorbate 80

70 g of γ -terpines are mixed with 930 g
30 polysorbate 80 and stirred until a clear and
homogeneous distribution is obtained. To accelerate
the mixing process, the mixture can be heated, for
example to up to 80°C. A 7% γ -terpine concentrate can
be dissolved in water to obtain a clear and stable

solution. To accelerate the dissolution process, the concentrate can be stirred in warm water at about 40°C.

- 5 Use of a different polysorbate, which is basically possible, requires a different distribution by weight in a concentrate of γ -terpines and polysorbate.

Example 4A (phosphatidylserin solubilizate):

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Material:

a)Phosphatidylserine powder (LECI - PS 90 ON of Degussa)

Characteristics:

15

LECI®-PS 90PN is a specially processed, phosphatidyl-serine-enriched, powdered soybean lecithin for use in nutritional supplements.

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Composition:

Phosphatidylserine and small amounts of other Phospholipids, having the following fatty acid distribution

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saturated fatty acids: 16-22 %

monounsaturated fatty acids: 9-14 %

polyunsaturated fatty acids: 62-71 %

of which:

linoieic acid: 57-65 %

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linolenic acid: 5-8 %

Specification:

Phosphatidylserine (PS): 88-92 %
lyso-Phosphatidylserine (LPS): max. 1 %
Phosphatidylcholine (PC): max. 2 %
Phosphatide acid (PA): max. 5 %
5 moisture: max. 1.5 %
peroxide value: max. 5

Microbiological Data: max. 1000 /g
total plate count: max. 50 /g
10 yeasts: max. 50 /g
moulds: negative /g
coliforms: negative /g
e-coli: negative /g
staphylococcus aureus: negative /g
15 salmonellae: negative /50g

b) Polysorbate 80

c) Glycerol 85%

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80 g phosphatidylserine powder is mixed with 510 g
polysorbate 80 and 410 g of glycerol and stirred until
a clear solution with homogeneous distribution is
obtained, and heated during the stirring to about
25 90°C. 7.2% phosphatidylserine concentrate prepared in
this manner, heated to about 40°C, can be dissolved
into a clear and stable solution.

Example 4B (phosphatidylserine solubilizate):

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Material:

a) Phosphatidylserine powder (LECI - PS 20 F of
Degussa)

Characteristics:

LECI®-PS 20F is a specially processed,
phosphatidylserine enriched, liquid soybean
lecithin combined with medium chain
triglycerides for nutritional supplements.

Composition:

Mixture of non-polar (triglycerides) and
polar (phospho- and glyco-) lipids, medium
chain triglycerides (MCT) and a small amount
of carbohydrates, having the following fatty
acid distribution

saturated fatty acids: 44-50
monounsaturated fatty acids: 6-9
polyunsaturated fatty acids: 40-48
of which:
linoleic acid: 36-42
linolenic acid: 3-6

Specification:

Phosphatidylserine (PS)	18-24	%
Phosphatidylcholine (PC)	min. 14	%
Phosphatidylethanolamine (PE)	max. 3	%
Phosphatidylinositol (PI)	max. 2	%
moisture	max. 1	%
iodine color value	max. 55	%
(10% in toluene)		
viscosity (25°C)	max. 10.0	Pas
peroxide value	max. 5	
toluene insolubles	max. 0.3	%

Microbiological Data:

	total plate count:	max. 1000/g
5	yeasts:	max. 100/g
	moulds:	max. 100/g
	coliforms:	negative /g
	e-coli:	negative /g
	staphylococcus aureus:	negative /g
10	salmonellae:	negative /25g

b)Polysorbate 80

c)Glycerol 85%

15 150 g of oily/viscous phosphatidylserine is mixed
with 600 g polysorbate 80 and 250 g glycerol and
stirred until a clear and homogeneous distribution is
obtained and during the stirring heated to about 90°C.
A 3.3% phosphatidylserine concentrate prepared in this
20 manner can be dissolved in water to give a clear
solution. To accelerate the process of dissolution
into water, the water can be heated, for instance, to
40°C.

25 When a different polysorbate is used, the mixing ratio
of the ingredients must be changed to obtain a clear
concentrate.

30 Example 5 (lanolin solubilizate):

Material:

- a) Lanolin (wax), Product No. 259543 of the firm Sigma-Aldrich
- b) Polysorbate 80

5 50 g lanolin is mixed with 950 g polysorbate 80 and it
is stirred while increasing the temperature of the
mixture to about 100°C until a clear and homogeneous
distribution is obtained. The concentrate obtained in
this manner contains 5% w/w lanolin. This 5% lanolin
10 concentrate can be dissolved in water to a clear and
stable solution. The dissolution is accelerated if the
concentrate is added to water heated to about 40°C and
stirred.

15 Example 6 (Linoleic acid triglyceride solubilizate):

Material:

- a) Conjugated linoleic acid triglyceride, marketed by
the firm Grünau Illertissen GmbH under the brand name
20 Selin CLA-TG.

General Information

Triglyceride on basis of conjugated linoleic
acid

25 Composition

Product Description

Color: slightly yellow
Odor / Taste: neutral - oily
30 Delivery form: liquid

Specification

Provisional specifications:

5 Acid number: max, 3
 Iodine number: 115-127
 Hydroxyl number: max. 10
 Water content: max. 0.2%
 Unsaponifiable: max. 1%

10 Fatty acid spectrum:
 < C16 max. 1%
 C16:1 max. 1%
 CI8 max. 3%
 C18:1 19-34%
 CI8:2 conj. 58 - 67%
 C18:2 2 - 9%
15 CI8:3 max. 1%
 > C13 max. 1%

Additional information

20 The use of conjugated linoleic acid (Selin®
 CLA) or conjugated linoleic acid triglyceride
 (Selin® CLA-TG) as a food supplement belongs
 largely to freely available state of the an.
 All the same, the GRÜNAU ILLERTISSEN GmbH
 feels it as its duty to draw the attention of
25 its customers to the following Industrial
 Property Rights of the Wisconsin Alumni
 Research Foundation (WARF);

b) Polysorbate 80

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50 g of oily, viscous linoleic acid triglyceride
is mixed with 950 g polysorbate 80 and stirred at
temperature of about 100°C until clear and homogeneous

distribution of the components is obtained. The concentrate prepared in this manner contains 5% w/w of the mentioned active substance. The concentrate can be dissolved in water to give a clear and homogeneous solution. The dissolution process is accelerated, if it is dissolved in water at about 40°C for instance.

Use of a different polysorbate, possible in principle, requires change in the weight proportions of the components of the concentrate. Regarding the importance of the conjugated linoleic acid triglyceride, reference is made to the document EP-B-579 901.

Example 7 (Citral solubilizate):

Material:

- a) Citral (Degussa, Lot No. 1000103751)
- b) Polysorbate 20
- c) Ethanol

At first, about 430 g of polysorbate 20 are heated to about 50°C to 60°C. In the hot polysorbate, about 70 g oily citral is introduced and stirred and during the stirring, the temperature of the mixture is increased to 85°C. The mixture is stirred at this temperature until it becomes homogenous. Thereafter about 500 g 96% ethanol is added to the cold mixture. The concentrate obtained in this manner is transparent, viscous and develops a mild lemon like odor. The concentrate contains about 7% w/w citral.

The concentrate is water soluble; to accelerate the process of dissolution, it is recommended to heat the water to about 40°C.

5 To prepare a 14% citral concentrate, in about 860
g of polysorbate 20, heated to about 50°C to about
60°C, about 140 g of oily citral is added. After
stirring it in completely, the temperature of the
mixture is increased during the stirring to about
10 85°C, and the stirring is continued further, until a
clear and homogeneous mixture is visible. After
cooling, one obtains a transparent, viscous 14% citral
concentrate with mild lemon like odor, which is
soluble in water. Here also, the dissolution into
15 water is accelerated, if water is heated mildly to
about 40°C.